

I Claim:

1. A vaccine for preventing gram negative infections and the effects of endotoxins which comprises a complex
5 obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide of the formula:
(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a
10 hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and
(c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids
15 which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.
- 20 2. A vaccine as defined in claim 1 wherein the peptide is a linear or cyclic peptides having units of the formula:
(a) $(A)_n$ wherein A is Lysine or Arginine and n is an integer with a value of 7 to 16;
(b) $(AB)_m$ wherein A is Lysine or Arginine and B is a
25 hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a value of 4 to 20; and
(c) $(ABC)_p$ wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids
30 which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a value of 4 to 20.
- 35 3. A vaccine as defined in claim 1 wherein the LPS is

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a'

derived from N. meningitidis.

4. A vaccine as defined in claim 1 wherein the LPS is derived from Salmonella typhi.

5 5. A vaccine as defined in claim 1 where the amount of peptide is from 2-10 to 2-5000 times the weight of the LPS.

6. A vaccine as defined in claim 1 wherein the peptide has units of the formula $(AB)_m$.

7 A vaccine as defined in claim 1 wherein the peptide has units of the formula $(ABC)_p$.

8. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys)₁₀. (SEQ ID NO: 1)

9. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys-Glu)₅. (SEQ ID NO: 4)

10. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys-Phe)₅. (SEQ ID NO: 5)

11. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Phe-Leu-Lys-Lys-Thr-Leu. (SEQ ID NO: 6)

12. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys-Phe-Leu)₂-Lys. (SEQ ID NO: 7)

13. A vaccine as defined in claim 1 wherein the peptide is of the formula:

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Sub B'

Sub B2

Sub B3

(Lys-Phe-Leu)₃-Lys. (SEQ ID NO: 8)

14. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Arg-Tyr-Val)₃. (SEQ ID NO: 9)

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15. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys-Phe-Phe)₃-Lys. (Seq ID NO: 10)

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16. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys-Leu-Leu)₃ (SEQ ID NO: 11)

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17. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys)₆(Phe-Lys)₂. (SEQ ID NO: 12)

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18. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Cys-(Lys)₅-Cys
S-----S. (SEQ ID NO: 13)

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19. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Cys-Lys-Phe-Lys-Lys-Cys
S-----S. (SEQ ID NO: 14)

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20. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Phe-Lys-Cys-Lys-Phe-Lys-Phe-Lys-Cys
S-----S. (SEQ ID NO: 15)

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21. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Leu-Lys-Cys-Lys-Leu-Lys-Leu-Lys-Cys
S-----S. (SEQ ID NO: 16)

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Sub
B3
Cont

Sub
B4

Arg-Thr-Arg-Cys-Arg-Phe-Lys-Arg-Arg-Cys
s-----s. (SEQ ID NO: 17)

Lys-Cys- (Lys-Phe-Lys)₂-Cys-Lys
s-----s. (SEQ/ID NO: 18)

Cys-(Lys)₄-(Phe)₄-Cys
S-----S. (SEQ ID NO: 19)

Cys- (Lys-Phe-Leu)₃-Lys-Cys
s-----s. (SEQ ID NO: 20)

Val-Lys-Ala-Leu-Arg-Val-Arg-Arg-Leu (SEQ ID NO: 21)

Lys-Ser-Leu-Ser-Leu-Lys-Arg-Leu-Thr-Tyr-Arg (SEQ ID NO:22)

Lys-Val-Arg-Lys-Ser-Phe-Phe-Lys-Val (SEQ ID NO: 23)

Phe-Leu-Lys-Pro-Gly-Lys-Val-Lys-Val (SEQ ID NO: 24)

30. A vaccine as defined in claim 1 wherein the peptide is

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a₃

of the formula:
Lys-Asp-Leu-Lys-Arg-Ile-Lys-Ile (SEQ ID NO: 25)

31. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu (SEQ ID NO: 26)

32. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 27)

33. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 28)

34. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Cys-Gln-Trp-Lys-Ser-Ser-Asp-Ile-Arg-Cys-Gly-Lys
S-----S (SEQ ID NO: 29)

35. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Cys-Lys-Phe-Leu-Lys-Lys-Cys
S-----S (Seq ID NO: 30)

36. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys (SEQ ID NO: 31)
S-----S

37. A vaccine as defined in claim 1 wherein the peptide is
of the formula:
Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 32)

38. A vaccine as defined in claim 1 wherein the peptide is
of the formula:

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B5

Sub
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Sub
B4
B5

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr-Lys
S - - - - - s (SEQ ID NO: 33)

5 39. A vaccine as defined in claim 1 wherein the peptide is
of the formula:

10 Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr
s - - - - - s (SEQ ID NO: 34)

40. A vaccine as defined in claim 1 wherein the peptide is of the formula:

15 Ile-Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys
s - - - - - s (SEQ ID NO: 35)

41. A vaccine as defined in claim 1 wherein the peptide is of the formula:

~~1~~ Ile-Lys-Thr-Lys-Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 36)

42. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 37)

43. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 38)

44. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Arg-Tyr-Val-Arg-Tyr-Val-Arg-Tyr-Val (SEQ ID NO: 39)

45. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Phe-Phe-Lys-Phe-Phe-Lys-Phe-Cys (SEQ ID NO: 40)

46. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu (SEQ ID NO:41)

47. A vaccine as defined in claim 1 wherein the peptide is of the formula:

(Lys)₆Phe-Leu-Phe-Leu (SEQ ID NO:42)

48. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Cys-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Cys
S-----S (SEQ ID NO: 43)

49. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 44)

50. A vaccine as defined in claim 1 wherein the peptide is of the formula:

Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 45)

51. A method for the preparation of a vaccine for prevention of gram-negative infections and the effects of endotoxins, said method comprising combining LPS with a stoichiometric excess of a peptide of the formula:

(a) (A)_n wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;

(b) (AB)_m wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and

(c) (ABC)_p wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

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cont

53. A vaccine as defined in claim 1 which contains an LPS peptide complex derived from more than one species of bacteria.

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Add B''

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